REMARKS/ARGUMENTS

This is in response to the Office Action mailed February 27, 2006 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants have amended claim 1 to include the limitation of claim 42, and have canceled claim 42. This amendment is believed to overcome the art rejections as set forth in ¶¶ 17- 28, as these rejections are not applied to claim 42.

Claim 1 has also been amended to specify that the mutant protein or pool of proteins has receptor-binding specificity for a receptor that is different from the receptor to which the wild type protein has receptor binding specificity. This amendment is believed to overcome the rejection under 35 USC § 112, second paragraph.

Claims 17, 18, 20, 27-29 have not been canceled since the restriction requirement as to these claims should be withdrawn under principles of unity of invention, since claim 1, to which they refer, is now allowable over the art. Similarly, claims 32 and 37 have been amended to include the same limitations as claim 1, and therefore these claims and the claims dependent thereon possess unity of invention and should recombined.

Withdrawn claims 30, 31 and 34-36 have been canceled without prejudice to Applicants right to pursue these claims in a timely filed divisional.

Based on the foregoing, the only issues remaining in this application are the rejections under 35 USC § 112, first paragraph for lack of written description and lack of enablement. Applicants again request reconsideration of the issues and withdrawal of the rejections.

The Examiner rejected claims 1-16 and 42 under 35 USC § 112, first paragraph, asserting a lack of written description. In this regard, the Examiner appears to focus in the number of specific examples of ribosome inactivating proteins and screening cell types, rather than on the **invention** as claimed. Further, the Examiner argues that failure to have characterized a significant number of products of the method means that there cannot be written description of the method. Applicants respectfully submit that this is an improper standard to be applied in the context of a written description rejection.

As a first matter, Applicants submit that it is appropriate to consider the written description issue in light of the decision of the Court of Appeals for the Federal Circuit in *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005). *Capon* involved an interference proceeding, in which the Patent Office Board of Appeals found that neither applicants disclosure met the written description requirement Both applications related to chimeric genes designed to combine DNA

encoding known antigen-binding domains and known lymphocyte-receptor protein into a unitary gene. Both applications claims such chimeric genes generically. The Patent Office Board of Appeals and Interferences held that there was a lack of written description because the applications claimed the invention in terms of function, instead of specific sequences or structures. In vacating and remanding the holding of the Board of Appeals, the Federal Circuit observed that "the 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge." 76 USPQ2d at 1084-5. In the present case, the Examiner has not looked at the "particular invention" as claimed to determine if there is a written description of that invention. This is improper.

The Examiner first argues that there is no written description of the genus of ribosome inactivating proteins because the specification does not contain an exhaustive list of every known heteromeric ribosome-inactivating protein. There is no question, however, that Applicants' specification disclosed both the generic name and a number of examples. Thus, a person skilled in the art would know, unequivocally, that Applicants understood their invention to include toxins within this genus at the time the invention is filed. Thus, the specification provides evidence of possession of the invention at the scope as claimed with respect to this element. Neither encyclopedic listing of examples nor specific experimental results are required.

The Examiner states that the lack of additional cell lines suitable for use with other toxins, particularly those not listed in the specification, is indicative of a lack of possession and thus a lack of written description of the entire scope of the invention. Again, this focuses to narrowly on the elements, and not on the invention as claimed. The present invention is a method. The method can be applied to cells different from CAMA-1, and this was clearly understood by the inventors as noted in the previous office action. The application of a written description rejection in this instance is plainly in error, since the purpose of the invention is to allow development of binding portions which may later be used with or without the associated to toxin, that bind to other types of cells. Indeed, it is interesting to note that had this standard been applied to patents claiming polymerase chain reaction (PCR) technology the claims would not have been allowed because the method would not have been demonstrated on enough species of targets sequences, with enough different primers.

On Page 8 of the Office Action, the Examiner states that "the practitioner would not envision that the application had process (sic, possession) of mutant proteins that have different receptor binding specificity." This is not relevant to the issue of written description, because Applicants are not claiming proteins, they are claiming a method of identifying proteins. In this regard, Applicants direct the Examiner's attention to Example 10 of the Examination Guidelines on Written Description (http://www.uspto.gov/web/menu/written.pdf) which clearly treating method and products differently and Example 18 concerning a method of making a protein.

Based on the foregoing, Applicants submit that the written description rejection is in error and should be withdrawn.

The Examiner also rejected claims 1-16 and 42 under 35 USC § 112, first paragraph, as lacking enablement. Applicants again traverse this rejection. Furthermore, Applicants point out that in applying the *Wands* factors the Examiner has not once addressed why any of the conclusions reached would lead to in a conclusion of undue experimentation.

The Examiner says that the invention is broad because the claim is "broadly drawn to making mutants of any heteromeric RIP toxin." What the Examiner has not said is why a person skilled in the art would have any difficulty or require undue experimentation to make such mutations. It is noted that this is a screening technique, in which many mutations are made and screened in order to find ones that have the desired properties.[1] There is no requirement in the claims, or for the use of the invention, that the mutations be made in any particular location or be of any particular type. Similarly, the Examiner says the claim is broad because the different receptor can be "virtually any biological molecule." Since the claims require no recognition of the nature of the different receptor, however, there is no explanation of why this breadth has anything to do with a need for undue experimentation. Indeed, one of the benefits of the invention is that you do not need to know what receptors are present on the screening cells, or to characterize this receptor in order to use the invention to identify a mutant protein that binds to such a receptor. Mere assertion of breadth, without more, is not a basis for asserting a lack of enablement. Thus, this *Wands* factor does not support the Examiner's position.

The Examiner also states that the amount of direction provided in the specification is limited, and therefore that undue experimentation would be required. This argument is misplaced, since claim 1 itself is essentially the instructions for performing the method of the invention.

Step A of claim 1 says to select a protein to be mutated. Step D says to use screening cells that are insensitive to the selected wild-type cytotoxic heteromeric protein toxin at a concentration used in the screening. In actuality, the cells are likely to be selected first, since the goal is likely to be to find a receptor binding part that will interact with a cell of interest. However, the point is clear. The protein and the cells are chosen in combination so that the cells

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[1] In this respect, the present invention is similar to making monoclonal antibodies in which many products may need to be tested to find one with the desired specificity. This level of testing was found not to be undue experimentation in *Hybritech Incorporated v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1996).

are insensitive to the wild type protein at the concentration used in the screening. No undue experimentation is required for this. If toxin sensitivity for a cell type is not already known, simply screening the cells against RIP toxins to find one that does not kill the cells establishes the pairing to use.

Step B says do mutations to the selected protein. Again, no reasons why this step would require undue experimentation have been offered. Step C says to clone the mutants, which again involves no undue experimentation. Step D says to screen the clone mutants against the cells, and selecting one that kills the cells. Finally, Step E says to make more of the protein of the selected type that killed the screening cells. Nowhere in the Office Action is there any explanation of how undue experimentation is required.

Applicants further note that the Examiner's citation of Battelli is irrelevant. It does not matter if there the correlation between RIP structure and toxicity is complex because mutant proteins are not designed in the present method (which might require more mechanistic understanding), but selected from among multiple mutations that can, if desired, be introduced at random. If the cells are killed by the mutant variant, then there is something about the mutant that allows it to interact with the screening cell and to result in toxicity. No extrapolation of cytotoxicity data or detailed understanding of the mechanism of cytotoxicity is required to practice the invention.

For these reasons, Applicants again submit that the rejection for lack of enablement is in error and should be withdrawn. The Examiner has offered no specific arguments that a person skilled in the art could not introduce mutations into a known toxin using the techniques described in the application, or test those mutations for toxicity using a screening cell line which is insensitive to the wild-type toxin, or recognize toxicity and choose to make more of the protein selected based on higher levels of toxicity, as compared to the wild type. This, being the case, Applicants submit that the Examiner has failed to present a *prima facie* case of lack of enablement of the claimed invention.

This application is believed to now be in form for allowance. Reconsideration and allowance are therefore urged.

Respectfully submitted,

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